L180 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:466702 CAPLUS
DOCUMENT NUMBER: 137:41737
TITLE: Combinations of sesquiterpene lactones and diterpene triepoxide lactones for synergistic inhibition of cyclooxygenase-2
INVENTOR(S): Babish, John G.; Howell, Terrence; Pacioretty, Linda
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002077299	A1	20020620	US 2001-919349	20010731 <--
US 2002076452	A1	20020620	US 2001-919506	20010731 <--

PRIORITY APPLN. INFO.: US 2000-222167P P 20000801
AB A novel formulation is provided that serves to inhibit the inflammatory response in animals. The formulation comprises, as a first component an effective amt. of diterpene triepoxide lactone species and an effective amt. of a second component of sesquiterpene lactone species or derivs. thereof, and provides synergistic anti-inflammatory effects in response to phys. or chem. injury or abnormal immune stimulation due to a biol. agent or unknown etiol. For example, a lotion designed to contain 0.1 % triptolide and 0.1% parthenolide was applied to affected areas of patients with acne rosacea and results showed improvement as compared with the placebo control.

L180 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:107101 CAPLUS
DOCUMENT NUMBER: 136:161354
TITLE: Terpene compound compositions exhibiting synergistic inhibition of the expression and/or activity of cyclooxygenase-2, and use as antiinflammatory agents
INVENTOR(S): Babish, John G.; Howell, Terrence M.; Pacioretty, Linda M.
PATENT ASSIGNEE(S): Ashni Naturaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009698	A1	20020207	WO 2001-US24053	20010801 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002077350	A1	20020620	US 2001-919510	20010731 <--

PRIORITY APPLN. INFO.: US 2000-222190P P 20000801
US 2001-919510 A 20010731

AB A formulation is provided that serves to inhibit the inflammatory response in animals. The formulation comprises, as a first component, a diterpene triepoxide lactone species or a sesquiterpene lactone species and, as a second component, at least one member selected from the group consisting of a diterpene triepoxide lactone species, a sesquiterpene lactone species, a diterpene lactone species, and a triterpene species or derivs. thereof, with the proviso that the same first component cannot also serve as the second component, and provides synergistic antiinflammatory effects in response to phys. or chem. injury or abnormal immune stimulation due to a biol. agent or unknown etiol.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L180 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:10197 CAPLUS
DOCUMENT NUMBER: 130:178519
TITLE: Validation and Subsequent Development of the Derek Skin Sensitization Rulebase by Analysis of the BgVV List of Contact Allergens
AUTHOR(S): Barratt, M. D.; Langowski, J. J.
CORPORATE SOURCE: SEAC Toxicology Unit, Unilever Research Colworth, Sharnbrook Bedford, MK44 1LQ, UK
SOURCE: Journal of Chemical Information and Computer Sciences (1999), 39(2), 294-298
CODEN: JCISD8; ISSN: 0095-2338
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The DEREK knowledge-based computer system contains a subset of approx. 50 rules describing chem. substructures (toxophores) responsible for skin sensitization. This rulebase, based originally on Unilever historical inhouse guinea pig maximization test data, has been subject to extensive validation and is undergoing refinement as the next stage of its development. As part of an ongoing program of validation and testing, the predictive ability of the sensitization rule set has been assessed by processing the structures of the 84 chem. substances in the list of contact allergens issued by the BgVV (German Federal Institute for Health Protection of Consumers). This list of chems. is important because the biol. data for each of the chems have been carefully scrutinized and peer reviewed, a key consideration in an area of toxicol. in which much unreliable and potentially misleading data have been published. The existing DEREK rulebase for skin sensitization identified toxophores for skin sensitization in the structures of 71 out of the 84 chems. (85%). The exercise highlighted areas of chem. where further development of the rulebase was required, either by extension of the scope of existing rules or by generation of new rules where a sound mechanistic rationale for the biol. activity could be established. Chems. likely to be acting as photoallergens were identified, and new rules for photoallergenicity have subsequently been written. At the end of the exercise, the refined rulebase was able to identify toxophores for skin sensitization for 82 of the 84 chems. in the BgVV list.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L180 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1976:505260 CAPLUS

DOCUMENT NUMBER: 85 105260

TITLE: Plant growth inhibitors of plant origin

AUTHOR(S): Schreiber, K.

CORPORATE SOURCE: Inst. Plant Biochem., Ger. Acad. Sci., Halle/Saale, Ger. Dem. Rep.

SOURCE: Environmental Quality and Safety, Supplement (1975), 3(Pesticides), 483-5
CODEN: EQSSDX; ISSN: 0340-4714

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Of the 524 compds. of plant origin tested in the wheat seedling test, 71 (14%) were highly active and 126 significantly active as growth retardants. Of the active compds., 58 (11%) were also active in the pea bioassay. Only 5 of the tested compds. were shown to be antagonists of gibberellin formation in Fusarium moniliforme. Twelve of the 28 naturally occurring lactones (mostly sesquiterpenoid .gamma.-lactones), 21 of 32

lichen constituents, and a relatively large no. of the steroids tested (28 of 90) were active.

L180 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1971:142092 CAPLUS
DOCUMENT NUMBER: 74:142092
TITLE: Correlation of structure and fragmentation modes of costunolide and its derivatives
AUTHOR(S): Sathe, R. N.; Deshpande, Mrs. N. R.; Kulkarni, G. H.; Kelkar, Govind R.; Das, K. Ganesh
CORPORATE SOURCE: Natl. Chem. Lab., Poona, India
SOURCE: Organic Mass Spectrometry (1971), 5(2), 197-202
CODEN: ORMSBG; ISSN: 0030-493X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mass spectral studies of costunolide and its lactone derivs., revealed general fragmentation modes involving the losses of 44, 55, 57, 59, 71, 73, and 83 mass units from the mol. ion. The genesis of these ions was established by high resolution, metastable transitions, and D labeling studies. Comparisons were made with the mass spectra of the C6-desoxy esters.

L180 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1963:482375 CAPLUS
DOCUMENT NUMBER: 59:82375
ORIGINAL REFERENCE NO.: 59:15314h,15315a-h
TITLE: Mexicanin. I. A new sesquiterpene lactone related to tenulin
AUTHOR(S): Dominguez, E.; Romo, J.
CORPORATE SOURCE: Univ. Nacl. Autonoma Mexico, Mexico City
SOURCE: Tetrahedron (1963), 19(9), 1415-21
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB cf. CA 55, 22365f. The mother liquors from isolation of helenalin from Helenium mexicanum evapd. and the residue crystd. from C6H6 gave 430 mg. product, m. 246-53.dblvert., recrystd. from CHCl2-MeOH to yield mexicanin I (I, R = H) (II), m. 257-60.degree., [.alpha.]20D 42.5.degree. (CHCl3). (All [.alpha.]D were detd. at 20.degree. in CHCl3.) II (150 mg.) in 4 ml. 1.1 Ac2O-C5H5N heated 1 hr. on a steam bath and dild. with H2O, filtered, and the ppt. crystd. from Me2CO.Et2O gave 130 mg. I (R = Ac) (III), m. 200-3.degree., [.alpha.]D 26.5.degree.. II (150 mg.) in 20 ml. MeOH treated with CH2N2 (from 2 g. MeNHCONHNO) in Et2O 30 min. at 20.degree. and the excess CH2N2 destroyed with a few drops of AcOH, the mixt. filtered off, and the residue washed with Et2O gave 90 mg. II

dipyrazoline, m. 185.degree. (decompn.). The nuclear magnetic resonance (n.m.r.) spectrum of III supported the assigned structure. II (200 mg.) in 8 ml. AcOH kept 1 hr. at 20.degree. with 150 mg CrO_3 in 5 ml. 1:4 H_2O-AcOH, the H_2O-dild. soln. extd. with $CHCl_3$, the ext. washed with H_2O, 5% Na_2CO_3, and H_2O, evapd., and the residue recrystd. repeatedly from Me_2CO-Et_2O gave dehydroisomexicanin I (IV), m. 232-5.degree., [.alpha.]D 129.degree.. II (300 mg.) in 150 ml. EtOAc hydrogenated over 80 mg. 10% Pd-C, the filtered soln. evapd., the oily residue crystd. from Et_2O, and the product crystd. from Me_2CO-C_6H_{14} yielded di-hydroisomexicanin I (V), m. 144-6 degree., [.alpha]D 150-4.degree.. The cyclo-pentanone bond was reduced but the remaining bond at C-7-C-11 resisted hydrogenation. The salient features of the spectra of II, III, IV, and V, particularly the sharp signal due to a tertiary Me group, strikingly resemble those of parthenin, tenulin, and helenalin, which possess an abnormal guaianolide nucleus. V (170 mg.) in 6 ml. AcOH treated with 150 mg. CrO_3 in 5 ml. 1:4 H_2O-AcOH, the mixt. kept 80 min. at 20.degree., dild. with H_2O and extd. with $CHCl_3$, the ext. washed with H_2O, dried (Na_2SO_4), and evapd., the residue crystd. from Me_2CO-C_6H_{14}, and recrystd. from Me_2CO-Et_2O gave dehydrodihydroisomexicanin I (VI), m. 173-5.degree., [.alpha.]D 184.degree.. VI (100 mg.) in 10 ml. AcOH refluxed 3 hrs. with 800 mg. powd. Zn, the filtered soln. dild. with H_2O and extd. with $CHCl_3$, the ext. washed with H_2O, 5% aq. NaOH, and H_2O, the dried ext. evapd., and the oily residue triturated with Et_2O gave 60 mg. needles recrystd. from Me_2CO-Et_2O to give dehydro-deacetyldihydroisotenulin (VII), m. 168-71.degree., [.alpha.]D 20 degree.. IV (100 mg.) similarly reduced gave 45 mg. VII, m. 147-9.degree., .alpha.]D 22..degree. Differences in m.p. were apparently due to solvation. II (500 mg.) in 80 ml. C_6H_6 refluxed 6 hrs. with 2 ml. $C_5H_{11}N$ and 2 ml. $PhCH_2SH$, the cooled mixt. washed with dil. HCl and H_2O, the dried soln. evapd., the residual oil (760 mg.) taken up in 70 ml. alc., the soln. refluxed 8 hrs. with 7 g. freshly prepd. Raney Ni with stirring, filtered, evapd., and the oily residue crystd. from Et_2O-C_6H_{14} and recrystd. from Me_2CO-Et_2O gave deacetyldihydroisotenulin (VIII, R = H) (IX), m. 194-6.degree., [.alpha.]D 139.degree.. IX (60 mg.) in 2 ml. 1:1 Ac_2O-C_5H_5N heated 1 hr. on a steam bath, the soln. poured into H_2O, extd. with $CHCl_3$, the ext. washed with dil. HCl, H_2O, dil. aq. NaOH, and H_2O, dried, evapd., and the oily residue crystd. from Et_2O and recrystd. from Et_2O-C_6H_{14} gave dihydroisotenulin VIII (R = Ac), m. 149-50.degree., [.alpha.]D 101.degree., 1770 cm.-1 IX (40 mg.) in AcOH oxidized with CrO_3 and the isolated product crystd. from Me_2CO-C_6H_{14} gave VII, m. 145-7.degree.. Accordingly, II is an "abnormal" guaianolide with asym. centers at C-1, C-5, C-8, and C-10 and lactone closure at C-8. The centers at C-6 and C-7 have the same configuration as in tetulin, but II differs from helenalin at C-6 and C-8 also, though both lactones have the same structural formula. II underwent a rearrangement in alk medium to yield products of the "neo" type. II (140 mg.) in 20 ml. MeOH refluxed 3 min. with 140 mg. KOH in 2 ml. H_2O, the

mixt kept 30 min. at 20.degree., acidified with AcOH, concd., dild. with H2O, extd. with CHCl3, and the H2O-washed ext. concd., treated with Et2O, and filtered off gave 70 mg. platelets, recrystd. from CHCl3-MeOH to give neomexicanin I (X, R = H) (XI) m. 259-63 degree., [.alpha.]D 10.degree.. The mother liquor from the 1st crystn. evapd., the oily residue crystd from Me2CO-C6H14, and the product recrystd. gave methoxydihydroneomexicanin I (XII), m. 168 70.degree., [.alpha.]D -27.degree.. Alk. treatment of II with KOH in tert-BuOH gave only XI. Acetylation of XI gave X (R = Ac), m. 170-2.degree. (Me2CO-Et2O), [.alpha.]D 3.degree.; n.m.r. spectrum showed similar signals to those reported for neohelenalin and neotenulin. III (500 mg.) in 60 ml. EtOAc hydrogenated over 60 mg. prereduced PtO2 4 hrs., the filtered soln. evapd., and the oily residue crystd. from Et2O and recrystd. from Et2O-C6H14 yielded 11-epidihydro-isotenulin, m. 109.degree., [.alpha.]D 48.degree.. Infrared, ultraviolet, and n.m.r. spectral data for most of the compds. were given.

L180 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1962:483404 CAPLUS
DOCUMENT NUMBER: 57:83404
ORIGINAL REFERENCE NO. 57:16665d-i,16666a-h
TITLE: Terpenoids. XXXII. Absolute configuration of junenol and levojunenol and synthesis of junenol from costunolide
AUTHOR(S): Shaligram, A. M.; Rao, A. S.; Bhattacharyya, S. C.
CORPORATE SOURCE: Nat. Chem. Lab., Poona, India
SOURCE: Tetrahedron (1962), 18, 969-77
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. CA 54, 22709d; 57, 13808e. The hydrocarbon-rich fraction (b0.5 90-102.degree.) of distd. vetiver oil chromatographed on acid-washed Al2O3 (grades III and II) and the tail portion crystd. from pert. ether and sublimed gave levojunenol (I), m. 65.degree., [.alpha.]D -57.degree. (I 1 18, all rotations in 95% alc.). I (298 mg.) heated (N atm.) 16 hrs. at 290.degree. with 446 mg. Se and the product taken up in petr. ether-C6H6, the concd. filtrate filtered through 30 g. Al2O3 (grade I) and eluted with petr. ether gave 228 mg. endalene, characterized as picrate, m. 95-6.degree., and s-trinitrobenzene deriv., m. 112.5-13.0.degree.. I (1.024 g.) in 25 ml. AcOH hydrogenated 4 hrs. with 40 mg. prereduced PtO2 and the product (970 mg.) sublimed gave dihydrolevojunenol (II), m. 115.degree.. [.alpha.]D .+-.0.degree. (C 2.6). I (970 mg.) in 60 ml. dry EtOAc at -5.degree. ozonized 5 hrs. with evolution of HCHO and the mixt. evapd. at 40.degree. in vacuo, the ozonide decompd. by heating in 30 ml. H2O on a steam bath 4 hrs. and the aq. layer extd. with Et2O, washed with aq. NaHCO3 and the neutral product isolated, the liquid residue (820 mg.) distd. at 135.degree. 0.1 mm. and the solid product sublimed gave 740 mg.

oxo alc. (III), C14H22O2, m. 43.degree., [.alpha.]D -11.5.degree. (c 2.00). The properties of I and its derivs. agree with those of an optical antipode of the dextrorotatory alc., junenol. III (420 mg.) in 4 ml. (HOCH2CH2)2O heated (N atm.) 2 hrs. with 400 mg. KOH and 0.7 ml. 85% N2H4.H2O at 110-15.degree. with occasional shaking and the H2O evapd. at 195.degree., the mixt. refluxed 4 hrs. at 190.degree. and the cooled product dild. with 30 ml. H2O, neutralized at 0.degree. with dil. HCl and extd. with Et2O, the ext. neutralized and the dried soln evapd., the product (383 mg.) dehydrogenated with 530 mg. Se at 280.degree. and the product chromatographed over 30 mg. Al2O3 (grade I) gave 2-Me2CHC10H7, characterized as s-trinitrobenzene deriv., m. 107.degree . Santanolide a (11.3 g., prepd according to Kovacs, et al., CA 50, 11285f, from L-santonin) in 100 ml. Et2O stirred at -10.degree. 1 hr. with addn. of 435 mg. LiAlH4 in 100 ml. dry Et2O and the mixt. stirred 2 hrs. before warming to 20.degree., the mixt. decompd. with H2O and extd. with Et2O gave 10.2 g. amorphous material showing a pos. Fehling test. The reduced product (3.17 g.) taken up in 14 ml. distd. (HOCH2CH2)2O and shaken 30 min. at 20.degree. with 6 ml. 85% N2H4.H2O, the soln. refluxed 2 hrs. (N atm.) with 3 g. KOH at 110-15.degree. and the H2O evapd. at 195.degree., the soln. refluxed 3 hrs. at 190.degree. and the cooled product dild. with 50 ml. H2O, repeatedly extd. with Et2O and the residue on evapn. (700 mg.) chromatographed over 30 g. Al2O3 (grade III), eluted with 200 ml. 9:1 petr. ether-C6H6 and the fraction sublimed gave 388 mg. alc., C15H28O (IV), m. 53-4.degree.. As expected, the infrared spectrum of IV differed from that of II, and the same series of reactions was applied to santanolide c (V). Costunolide (21.4 g., m. 106.degree.), [.alpha.]D 128.degree. in 200 ml. AcOH contg. 10 ml. 65% HClO4 hydrogenated with prereduced PtO2 and the filtered soln. concd. to 70 ml., neutralized with Na2CO3 and extd. with Et2O gave 6.3 g. V, m. 153-4.degree. (alc.), [.alpha]D 54.9.degree., also prepd. by hydrogenating a mixt. of costunolide and dehydrocostus lactone. V (9.9 g.) in 100 ml. Et2O partially reduced with 500 mg. LiAlH4 in 100 ml. Et2O and totally reduced by Huang Minlon reduction gave material, purified by chromatography and sublimation to yield 379 mg. alc. (VI), m. 115.degree., [.alpha.]D .+-. 0.degree. (c 1.52), giving an infrared spectrum completely superimposable on that of II, and an identical n.m.r. spectrum, showing that VI and II are either identical or enantiomorphic. Mixed m.p. of VI and II gave a 20.degree. depression and the lack of identity was confirmed by measurement or rotatory dispersion curves. The mol. rotation difference (.DELTA.M = -129.degree.) between I and II is neg. but of the same magnitude as that between junenol (VII) and VI, which is of the same sign as that between eudesmol and dihydroeudesmol. Accordingly the abs. configuration of VII, I, and II can be depicted. I is the 1st naturally occurring eudesmanic compd. contg. both .alpha.-oriented C-10 Me and C-7 Me2CH groups. The acid cyclization of dihydrocostunolide (VIII) gave a mixt. of 2 closely related lactones,

the endocyclic unsatd. lactone (IX) and the exocyclic unsatd. isomeride (X), sepd. by column chromatography. VIII (m. 77.degree., [.alpha.]D 113.degree.) cyclized in AcOH and Ac2O and the mixt. (62 g.) chromatographed on 2.4 kg. Al2O3 (grade III) and eluted successively with 10 l. petr. ether, 6 l. 1:1 petr. ether-C6H6, 6 l. C6H6, 6 l. alc., and 6 l. AcOH gave 27 g. fraction, m. 128.degree.; 0.8, 0.5, and 0.5 g. fraction, m. 60.degree.; and 24.5 g. fraction, m. 132.degree.. The 1st fraction repeatedly recrystd. from alc. and C6H14 and sublimed gave IX, m. 140.degree., [.alpha.]D 85.degree. (c 1.402, CHCl3), hydrogenated in AcOH with prereduced PtO2 to give V. The last fraction recrystd. from C5H12 and sublimed gave the lactone X, m. 140.degree. [.alpha.]D 140.degree. (c 3.5, CHCl3), hydrogenated in AcOH with prereduced PtO2 to give santanolidea. X (1.1 g.) in 30 ml. dry EtOAc ozonized 5 hrs. at -5.degree. with evolution of HCHO, the product crystd. from alc. and sublimed at 150.degree /0.05 mm. gave 800 mg. oxo lactone (XI), m. 220.degree. [.alpha.]D 71.48.degree. (c 1.525, CHCl3). X (7.15 g.) in 150 ml. anhyd. Et2O at -10.degree. stirred 1 hr. with addn. of 420 mg. LiAlH4 in 100 ml. Et2O and the mixt. stirred 2 hrs. at -10.degree. and 1 hr. at 20.degree., the washed and dried Et2O layer evapd. in vacuo and the partially reduced lactone (6.8 g.) heated 5 min. on a steam bath in 40 ml. (HOCH2CH2)2O and 11 ml. 85% N2H4.H2O, the clear soln. kept 30 min. at 20.degree. and refluxed 2 hrs. at 110-15.degree. with 6 g. KOH, treated at 60.degree. with 20 ml. dry C6H6 and the C6H6 carefully evapd. at 130.degree. the procedure repeated 3 times and the H2O-free soln. refluxed 2 hrs. at 150.degree., the cooled mass dild. with 50 ml. H2O and extd. with Et2O, the product (800 mg.) chromatographer on 30 g. Al2O3 (grade III) and the column eluted with 200 ml. 9:1 petr. ether-C6H6, the fraction crystd. from petr. ether and sublimed gave VII, m. 61-2.degree., [.alpha.]D 51.degree. (C 2.45). Ultraviolet, infrared, and nuclear magnetic resonance spectra were given.

L180 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1962:423334 CAPLUS
DOCUMENT NUMBER: 57:23334
ORIGINAL REFERENCE NO : 57:4699b-g
TITLE: Conversion of costunolide to junenol
AUTHOR(S): Shaligram, A. M ; Rao, A. S.; Bhattacharyya, S. C.
CORPORATE SOURCE: Natl. Chem. Labs., Poona, India
SOURCE: Chem. Ind. (London) (1961) 671
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB (All [.alpha.]D in EtOH.) Previously (CA 54, 22709d) the abs. configuration was established of the enantiomeric sesquiterpene alcs. junenol (I) and levojunenol (II), on the basis of conversion of santanolide c (III) to dihydrojunenol (IV). The structure and conversion

of the lactone V to dextrorotatory I was now described. Cyclization of VI gave a product (VIa), m. 117.degree., much lower than that of the lactone (VII), previously (CA 54, 3489d) obtained by cyelization of VI. Chromatography of Via gave VII, m. 140.degree., [.alpha.]D 85.degree. (c 1.402), giving III on catalytic hydrogenation, giving no CH2O on ozonolysis, this structure also being in agreement with its infrared (v 790 and 1794 cm.-1) and ultraviolet spectra (.epsilon.210 287, .epsilon.2151435, .epsilon.220 385), and an isomer (V), m 140.degree., [.alpha.]D 140.degree. (c 3.55), this structure being assigned on the basis of infrared (v 885, 1633, and 1764 cm.-1) and ultraviolet spectra (.epsilon 210 377, .epsilon.215 120, .epsilon.220 75), giving santanolide a on catalytic hydrogenation, giving on ozonolysis CH2O (dimedon deriv. m. 189.degree.) and the oxo lactone (VIII), m. 210.degree., [.alpha.]D 71.degree. (c 1.525). V was converted to d-I as described previously for the conversion of III to IV. d-I m. 61-2.degree., [.alpha.]D 51.degree. (c 2.45), its infrared spectrum being identical with that of II.

L180 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1962:38646 CAPLUS
DOCUMENT NUMBER: 56:38646
ORIGINAL REFERENCE NO.: 56:7368c-i
TITLE: CXXXI. Isolation and structure of costunolide , balchanolide, isobalchanolide, and hydroxybalchanolide, sesquiterpenic lactones of germacrane type from Artemisia balchanorum
AUTHOR(S): Krasch, H.; Herout, V.; Suchy, M.; Sorm, F.
CORPORATE SOURCE: Ceskoslov. Akad. Ved., Prague
SOURCE: Collection Czechoslov. Chem. Communs. (1961), 26, 2612-23
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB Costunolide (I), m. 106.degree. (MeOH), [.alpha]20D 128.degree. (c 10.5. CHCl3), isobalchanolide (II), m. 133.degree. (iso-Pr2O-Me2CO), [.alpha.]20D 122.degree. (c 2.08, CHCl3), balchanolide (III), m. 154.degree. (iso-Pr2O-Me2CO), [.alpha.]20D 183 degree. (c 1.84, CHCl3), and hydroxybalchanolide (IV), m. 163.degree. [.alpha.]20D 105.degree (c 2.71, EtoH). Hydrogenation of I in MeOH over 5% Pd on C gave dihydrocostulolide (V), m. 79-80.degree. (MeOH). Hydrogenation of I in AcOH over PtO2 gave oily hexahydrocostunolide. If 2 drops of 70% HClO4 were added to the mixt., the H uptake amounted to 2.0 double bonds and santanolide C (VI) was the chief product, m. 155.degree. (EtOH), [.alpha.]20D 50.1.degree. (c 4.0, CHCl3), along with 2 compds., m. 114.degree. (MeOH) and m. 79.degree., isolated by chromatography. Refluxing V with AcOH and Ac2O, evapg. the mixt , and crystg. from MeOH

gave a compd., m. 122.degree., whose recrystn. from 1:5 C6H6-petr. ether gave 3-santenolide (VII), m. 135.5.degree.. Hydrogenation of VII in AcOH over PtO2 (H uptake amounted to 1.05 double bonds) followed by crystn. and chromatography gave VI along with santanolide A, m. 153.degree. (80% aq. EtOH). The location of the double bonds in I (CA 54, 3489b) was verified by ozonization of V in AcOH and decompn. of the ozonides in boiling HNO3: the chief product, a lactonedicarboxylic acid, Rf 0.38 (BuOAc-2% HCO2H), was identical with that prepd earlier from artabsin. Acetylisobalchanolide, m. 139-40.degree., [.alpha.]20D 18.5.degree (c 1.8, CHCl3), was hydrogenated in MeOH over PrO2 to give tetrahydroacetylisobalchanolide (VHI), m. 125.degree. (iso-Pr2O), identical with tetrahydroacetylbalchanolide, prepd. earlier. Hydrolysis of VIII with K2CO3 in MeOH followed by oxidn. of the oily product with CrO3 in AcOH gave an oxo lactone, C15H24O3, m 136.5.degree. (iso-Pr2O), identical with that prepd. earlier from arctiopicrin and cnicin. Oxidn. of II-IV with satd. aq. KMnO4 gave a mixt. of (CH2CO2H)2 and MeCOCH2CH2CO2H, identified by paper chromatography. Oxidn of III with CrO3 in C5H5N gave an oxo lactone, C15H20O3, m. 110.degree. (iso-PrO2). Hydrogenation of IV in AcOH over PtO2 gave tetrahydrohydroxybalchanolide C15H26O4, m. 101.degree. (iso-Pr2O-Me2CO), whose oxidn. with CrO3 in AcOH gave a hydroxy oxo lactone, C15H24O4 (IX), m. 127.degree. (isoPr2O-Me2CO). Structures of II-IV and some of their derivs. were suggested. II and III differ in the location of the double bonds, or, in their steric arrangement (cis-trans-isomerism) only.

L180 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1961:137670 CAPLUS
DOCUMENT NUMBER: 55:137670
ORIGINAL REFERENCE NO.: 55:26013g-i,26014a-i,26015a-i,26016a-d
TITLE: Cedrol: stereochemistry and total synthesis
AUTHOR(S) Stork, Gilbert; Clarke, Frank H , Jr.
CORPORATE SOURCE: Columbia Univ.
SOURCE: J. Am. Chem Soc. (1961), 83, 3114-25
CODEN: JACSAT, ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB The total stereospecific synthesis of natural cedrol (I) was described. Me2C(CN)CH(CN)CO2Et (II), b0.01 about 99-114 degree., b4 120-7.degree. (with decompn), (250 g.) in 232 g. Me3COH treated with 87 g. CH2:CHCN and 5 0 cc. 40% choline in MeOH, the mixt. kept 6 hrs. at 0.degree., 18 hrs. at room temp., and 40 hrs. at 50 degree., cooled until crystals of Me3COH appeared, the top layer evapd. on the steam bath in vacuo, the combined residue and bottom layer dild. with Et2O, washed, evapd., the combined residues (638 g.) from 2 runs dissolved in 1300 cc. concd. HCl and 1300 cc. H2O, the soln. refluxed 48 hrs , evapd. on the steam bath, cooled,

filtered, evapd. to dryness, the residue treated with abs. EtOH, filtered, the filtrate (3500 cc.) refluxed 4.5 days with stirring with 700 cc. concd. H2SO4, 1 l. of EtOH distd., the residual soln. cooled, poured into satd. aq. NaCl, the oily layer worked up with Et2O, and distd. gave 480 g. Me2C(CO2Et)CH(CO2Et)(CH2)2CO2Et (III), b0.01 about 154-6.degree., and 158 g. residue, which hydrolyzed and reesterified gave more III. III refluxed 3 hrs. in C6H6 with powd. Na yielded 64% di-Et 3,3-dimethylcyclopentan-2-one-1,4-dicarboxylate (IV), b 132-3.degree. (in vacuo). PhCH2OH (34.0 g.), 48 g. MeCHBrCO2H, and about 0.5 g. p-MeC6H4SO3H in 150 cc. C6H6 refluxed 18 hrs. with azeotropic removal of H2O gave 55.5 g. MeCHBrCO2CH2Ph (V), b7 139-41.degree. IV (50.0 g.) in 80 cc. dry C6H6 and 6.0 g. NaH in 100 cc. dry C6H6 refluxed until the H evolution ceased, decanted, the soln. distd. to remove 155 cc. C6H6, treated with the Na salt of 47.5 g. V in 100 cc. dry HCONMe2, the mixt. heated at 50.degree. under N, kept 1 week, combined with the soln. of a 2nd run from 71 .1 g. IV, and worked up yielded 179 g. 1-PhCH2 ester (VI) of the HO2CCHMe deriv. (VII) of IV, b. 175-92.degree. (in vacuo). VI (77.0 g.) in 150 cc. EtOAc hydrogenolyzed during 35 min over 8.0 g 10% Pd-C at an initial pressure of 50.0 lb. yielded 47.0 g. VII, prisms, m 113-15.degree. (cyclohexane). Na salt (11.6 g.) of VII in 100 cc. dry C6H6 contg 1.0 cc. C5H5N with 15 cc. (COCl)2 added slowly to excess CH2N2 in Et2O from 45 g. H2NCON(NO)Me, the mixt. kept 1 hr. at 0.degree., evapd. on the steam bath, and the residual crude diazoketone treated in 150 cc. dry Et2O with cooling with dry HCl gave 10.7 g. 1-ClCH2COCHMe deriv (VIII) of V, m. 72-3.degree. (cyclohexane). VIII (19.2 g.) and 20 g. powd. KI in 250 cc. AcOH treated slowly with stirring at 25.degree. with 100 g. Zn dust, stirred 6 hrs., dild. with 50 cc H2O, stirred overnight, filtered, the filtrate evapd , the residue partitioned between H2O and Et2O, and the Et2O soln. worked up gave 17.1 g. 1-AcMeCH deriv. (IX) of V, m. 55-60.degree (petr. ether); semicarbazone m. 191-3.degree. (aq. EtOH). Crude IX (4.3 g.) in 30 cc. dry Me3COH and 0.7 g. K in 70 cc. dry Me3COH refluxed 3 hrs. under N, dild. with H2O, and extd. with Et2O gave 1.47 g. mobile oil; a 0.4-g. portion, 0.45 g. semicarbazide, 1.65 cc. C5H5N, and 8 cc. EtOH refluxed 1.5 hrs. and kept overnight yielded the semicarbazone of X, m. 174-6.degree. (EtOAc-cyclohexane) IX (20.1 g.) and 3.0 g. K in 300 cc. dry Me3COH kept 10 min. at room temp. gave 18.6 g. crude aldol, which, refluxed 1 hr. with 2.0 g. p-MeC6H4SO3H.H2O in 400 cc. C6H6, yielded 15.2 g. XI, m. 46-56 degree. (petr. ether); 23.6 g. crude XI recrystd. twice from petr. ether gave 10.8 g. of 1 isomer, m. 65-7.degree., of XI. XI (504 mg.), m 65-7.degree., in 16 cc. abs. EtOH hydrogenated 20 min. at 25.4.degree. over 136 mg. 10% Pd-C yielded 325 mg. XII, m. 33.5-35.0 degree. (petr. ether); 2,4-dinitrophenylhydrazone (XIII) m. 160-1.degree.; recrystd from EtOAc-EtOH, it gave needles, which slowly changed to prisms on standing in the soln. XI (307 mg.) in 2 cc. dry tetrahydrofuran and 15 cc. dry liquid NH3 treated with stirring with 15-20 mg. Li and then with 0.6 g. NH4Cl, the NH3 evapd., and the residual

yellowish oily XII (271 mg.) chromatographed from petr. ether on Al2O3 yielded oily colorless XII; XIII m. 152-4.degree (EtOAc-EtOH). XII (655 mg.) in 10 cc 80% EtOH refluxed 36 hrs. under N with 2.0 g. KOH, poured into H2O, washed with Et2O, acidified with concd. HCl, extd. with Et2O, the gummy residue (528 mg.) from the ext. refluxed 3 hrs. with 6 cc. Ac2O, evapd. under a stream of N, and the dark residue sublimed in vacuo at 160-70.degree gave 174 mg. anhydride (XIV), prisms, m. 171-3.degree. (Et2O). The XIV refluxed 20 hrs. with 6 cc. 50% aq. dioxane and the oily product treated with MeCHN2 from 5 cc. EtO2CN(NO)Et yielded 102 mg. XII; XIII m. 159-61.degree XII (1.03 g.) in 10 cc CHCl3 and 1.0 cc. (CH2SH)2 satd with dry HCl and kept at 0.degree. overnight yielded 0.86 g. XV, m. 75-6.degree. (pentane). XV (1.32 g.) in 125 cc. abs. EtOH stirred 15 hrs at reflux with 50 g. Raney Ni alloy gave 0.86 g. di-Et ester (XVI) of dl-norcedrenedicarboxylic acid (XVII), mobile oil. XVII (0.82 g.) and 2.0 g. KOH in 10 cc. 95% EtOH refluxed 24 hrs., poured into H2O, and acidified with 10 cc. concd. HCl gave 0.62 g. XVII, m. 221-3.degree. (Et2O-pentane). XVII (300 mg.) in Me2CO with 410 mg. quinine in acetone yielded 252 mg. quinine salt (XVIII) of (-)-XVII, m. 209-10.degree. (CHCl3Me2CO), [.alpha.]27D -122.degree. (c 1.00, CHCl3). XVII (121 mg.) shaken 15 min. with 5 cc. 6N HCl gave 46 mg. (-)-XVII, m. 212-13.degree., [.alpha.]27D -38.9 .+-. 1.5.degree (c 1.08, Me2CO); natural (-)-XVII m. 213-14.degree., [.alpha.]27D -38.3 .+-. 1.0.degree. (c 1.09, Me2CO) (-)-XVII (10.00 g.) with excess CH2N2 in Et2O yielded 10.59 g. XIX (R = CO2H) (XX), bl 95-132.degree.. XX (10.5 g.) and 2.4 g. KOH in 35 cc. abs. EtOH refluxed 2 hrs. gave about 2 g. unchanged XX and 6.20 g. XIX (R = CO2Me) (XXI), m. 129-32.degree.. XXI (8.05 g.) and 20 cc. (COCl)2 kept 1.5 hrs. at room temp., dild., evapd with C6H6, the residual XIX (R = COCl) treated 1 hr. with CH2N2 from 45 g. H2NCON(NO)Me in Et2O, the resulting crude XIX (R = CON2) in 50 cc. dry Et2O satd. with dry HCl, evapd. in vacuo on the steam bath, the XIX (R = COCH2Cl) treated with cooling and stirring with 9 g. KI in 100 cc. 80% AcOH and 45 g. powd. Zn, and the mixt. stirred at room temp. overnight yielded 7.73 g. crude XIX (R = Ac) (XXII), 2,4-dinitrophenylhydrazone m. 140-2 degree. (cyclohexane). XXII (7.73 g.) and 3.0 g KOH in 120 cc. dry Me3COH refluxed 3 hrs. yielded 4.90 g. XXIII, m. 202-4.degree. (dioxane). XXIII (2.00 g.) refluxed 17 hrs. with stirring with 2.00 g. LiAlH4 in 50 cc. dry Et2O gave 1.91 g. (crude) XXIV, m. 120-1.degree. (cyclohexane). Crude XXIV oxidized with CrO3-C5H5N and the crude product chromatographed on Al2O3 yielded XXV; 2,4-dinitrophenylhydrazone m. 146-7.degree.. XXIII (2.84 g.) in 50 cc abs EtOH contg. 0.10 g. p-MeC6H4SO3H H2O distd. during 4 hrs. to remove 53 cc. distillate gave 2.82 g. oily mixt. of the enol ethers; the crude mixt. in 25 cc. dry Et2O reduced with 1.0 g. LiAlH4 in 150 cc. Et2O and the crude product (2.45 g.) refluxed 1.5 hrs with 0.20 g. p-MeC6H4SO3H.H2O in 50 cc. C6H6 yielded 508 mg. XXIV. XXIII (5.21 g.) in dry Et2O reduced with 7.77 g. LiAlH4 in 250 cc. dry Et2O, the crude foamy product (4.11 g.) treated 17 hrs. at room temp. with 8.43 g. CrO3 in 84

cc. C5H5N, the mixt. poured into 750 cc. Et2O, filtered, and the filtrate worked up gave 2.81 g. pale yellow oily aldehyde-ketone; a 2.50-g. portion refluxed 1.45 hrs. with 12.5 g. KOH in 500 cc. H2O at about 50.degree. and 90 mm., extd with Et2O, and the crude oily product (2.02 g.) chromatographed on Al2O3 yielded 1.47 g. XXVI; 2,4-dinitrophenylhydrazone, brilliant red prisms, m. 164-7.degree. (MeOH). XXVI (527 mg.) in 10 cc. abs. EtOH hydrogenated 1 hr. at 23.degree. gave 524 mg. oily XXV; 2,4-dinitrophenylhydrazone, yellow needles changing to prisms on standing in soln., m. 146-7.degree. (MeOH). XXIV (219 mg.) in 2.2 cc. C5H5N treated 23 hrs. at room temp. with 224 mg. CrO3 in 2.2 cc. C5H5N yielded 190 mg. XXV. XXV (164 mg.) reduced during 17 hrs. with 0.40 g. LiAlH4 in 30 cc. Et2O gave 140 mg. XXIV. XXV (446 mg.) in dry Et2O added slowly to MeLi from 1.8 g. Li and 6 cc. MeI in 40 cc. dry Et2O and the mixt. refluxed 18.5 hrs. with stirring gave I, collected in 4 fractions: 380 mg., m. 80-1.degree.; 340 mg., m. 83-7.degree.; 284 mg., m. 85-7.degree.; 215 mg., m. 86-7.degree., needles, [.alpha.]28D 10.5 .+-. 0.8.degree. (c 5.00); natural I m. 86-7.degree., [.alpha.]28D 9.9 .+- 0.4.degree. (c 5.00, CHCl3).

L180 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1950:711 CAPLUS
DOCUMENT NUMBER: 44:711
ORIGINAL REFERENCE NO.: 44 138f-i,139a-b
TITLE: Helenalin. I. Isolation and properties
AUTHOR(S): Adams, Roger; Herz, Werner
SOURCE: J. Am. Chem. Soc. (1949), 71, 2546-51
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. Clark, C.A. 30, 8236.2. Helenalin (I), C15H18O4, was isolated from Helenium microcephalum by the method of C. in av. yields of 0.38% and, crystd. 3 times from abs. EtOH, m. 176-8.degree.; the residue, crystd. 3 times from abs. EtOH, m. 165.5-6.degree., [.alpha.]D25 -102.8.degree. (0.0728 g. in 2 ml. 95% EtOH); the infrared spectrum is identical with that of C.'s prepn. The Ac deriv. (II), m. 179.5-80.5.degree., absorption max. at 221 and 316 m.mu. (.epsilon. 12, 600 and 61). o-Bromobenzoyl deriv. of I, m. 162-3.degree., p-nitro-benzoyl deriv. of I, with 0.5 mol. C6H6, m. 111.degree.; 3,5-dinitrobenzoyl deriv., with 0.5 mol. C6H6, m. 213.degree.. Tetra-hydrohelenalin (III), m 175-6.degree., infrared spectrum given; Ac deriv. (IV), m. 145.degree. (prepd. by acetylation of III or by reduction of II in AcOEt over Pt oxide); the spectra of III and IV are similar [absorption max. at 287 m.mu. (.epsilon. 36)]. IV (115 mg.) and 64 mg. piperonal in 2 ml. abs. EtOH, treated with 5 ml. satd. EtOH-HCl and kept 18 hrs., give the piperonylidene deriv. of II, C25H25O7Cl, pale yellow, m. 214.degree.. I (50 mg.) in 1 ml. AcOH, treated with 1.03 g. Br in 15 ml.

AcOH at room temp., gives 71 mg. dibromohelenalin (V), decomp. 130.degree.; recrystn. of V from 50% EtOH or 50% AcOH gives bromohelenalin, m. 164.5.degree., absorption max. at 248 and 314 m.mu. (.epsilon. 6300 and 97); reduction over Pt oxide gives III. II and Br in Ac-OH, irradiated with an elec. light, give a di-Br deriv , decomp 153-4.degree.; boiled 0.5 hr. with 50% EtOH, it gives the Br deriv., m. 153.5.degree.. I and NH2OH.HCl in abs. EtOH contg. AcONa, refluxed 16 hrs., give the compd. C15H22N2O5, amorphous, m. 200-3.degree. (decompn.). I (1 g) and 4 g. (iso-PrO)3Al in 20 ml. iso-PrOH, refluxed 5 hrs., the solvent removed by slow distn., 20 ml. iso-PrOH added, the distn. continued until the test for Me2CO is neg., the product decompd. with 25 ml. 10% H2SO4, and extd. with ether, give 100 mg. of the compd., C15H20O4, b0.1 200-30.degree. (bath temp.), it did not yield a solid ester; in 1 expt. there resulted 29 mg. of a compd., m. 196-201.degree., which may be an intramol. oxidation-reduction product. I and O3 give 50-60% HCHO; II gives 45% HCHO. Chem. and phys. evidence establishes the presence of the grouping RCOCH:CR2, possibly a part of a 5-membered ring, and makes likely the presence of a lactone ring. These functional groups account satisfactorily for all 4 O atoms and for 1 of the double bonds. The other double bond is unconjugated and part of a terminal CH2 group.

L189 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:107101 CAPLUS
DOCUMENT NUMBER: 136:161354
TITLE: Terpene compound compositions exhibiting synergistic inhibition of the expression and/or activity of cyclooxygenase-2, and use as antiinflammatory agents
INVENTOR(S): Babish, John G.; Howell, Terrence M.; Pacioretty, Linda M.
PATENT ASSIGNEE(S): Ashni Naturaceuticals, Inc., USA
SOURCE: PCT Int. Appl , 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009698	A1	20020207	WO 2001-US24053	20010801

W AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,

RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002077350 A1 20020620 US 2001-919510 20010731
PRIORITY APPLN. INFO. US 2000-222190P P 20000801
US 2001-919510 A 20010731

AB A formulation is provided that serves to inhibit the inflammatory response in animals. The formulation comprises, as a first component, a diterpene triepoxide lactone species or a sesquiterpene lactone species and, as a second component, at least one member selected from the group consisting of a diterpene triepoxide lactone species, a sesquiterpene lactone species, a diterpene lactone species, and a triterpene species or derivs. thereof, with the proviso that the same first component cannot also serve as the second component, and provides synergistic antiinflammatory effects in response to phys. or chem. injury or abnormal immune stimulation due to a biol. agent or unknown etiol.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L189 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:466702 CAPLUS
DOCUMENT NUMBER: 137:41737
TITLE: Combinations of sesquiterpene lactones and diterpene triepoxide lactones for synergistic inhibition of cyclooxygenase-2
INVENTOR(S): Babish, John G.; Howell, Terrence; Pacioretty, Linda
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002077299	A1	20020620	US 2001-919349	20010731
US 2002076452	A1	20020620	US 2001-919506	20010731

PRIORITY APPLN. INFO. US 2000-222167P P 20000801

AB A novel formulation is provided that serves to inhibit the inflammatory response in animals The formulation comprises, as a first component an effective amt. of diterpene triepoxide lactone species and an effective amt. of a second component of sesquiterpene lactone species or derivs.

thereof, and provides synergistic anti-inflammatory effects in response to phys. or chem injury or abnormal immune stimulation due to a biol. agent or unknown etiol. For example, a lotion designed to contain 0.1 % triptolide and 0.1% parthenolide was applied to affected areas of patients with acne rosacea and results showed improvement as compared with the placebo control.

L189 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:10197 CAPLUS
DOCUMENT NUMBER: 130:178519
TITLE: Validation and Subsequent Development of the Derek Skin Sensitization Rulebase by Analysis of the BgVV List of Contact Allergens
AUTHOR(S): Barratt, M. D.; Langowski, J. J.
CORPORATE SOURCE: SEAC Toxicology Unit, Unilever Research Colworth, Sharnbrook Bedford, MK44 1LQ, UK
SOURCE: Journal of Chemical Information and Computer Sciences (1999), 39(2), 294-298
CODEN: JCISD8; ISSN: 0095-2338
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The DEREK knowledge-based computer system contains a subset of approx. 50 rules describing chem. substructures (toxophores) responsible for skin sensitization. This rulebase, based originally on Unilever historical inhouse guinea pig maximization test data, has been subject to extensive validation and is undergoing refinement as the next stage of its development. As part of an ongoing program of validation and testing, the predictive ability of the sensitization rule set has been assessed by processing the structures of the 84 chem. substances in the list of contact allergens issued by the BgVV (German Federal Institute for Health Protection of Consumers). This list of chems. is important because the biol. data for each of the chems. have been carefully scrutinized and peer reviewed, a key consideration in an area of toxicol. in which much unreliable and potentially misleading data have been published. The existing DEREK rulebase for skin sensitization identified toxophores for skin sensitization in the structures of 71 out of the 84 chems. (85%). The exercise highlighted areas of chem. where further development of the rulebase was required, either by extension of the scope of existing rules or by generation of new rules where a sound mechanistic rationale for the biol. activity could be established. Chems. likely to be acting as photoallergens were identified, and new rules for photoallergenicity have subsequently been written. At the end of the exercise, the refined rulebase was able to identify toxophores for skin sensitization for 82 of the 84 chems. in the BgVV list.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L189 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1976:505260 CAPLUS
DOCUMENT NUMBER: 85:105260
TITLE: Plant growth inhibitors of plant origin
AUTHOR(S): Schreiber, K.
CORPORATE SOURCE: Inst. Plant Biochem., Ger. Acad. Sci., Halle/Saale, Ger. Dem. Rep.
SOURCE Environmental Quality and Safety, Supplement (1975), 3(Pesticides), 483-5
CODEN: EQSSDX; ISSN: 0340-4714
DOCUMENT TYPE: Journal
LANGUAGE English
AB Of the 524 compds. of plant origin tested in the wheat seedling test, 71 (14%) were highly active and 126 significantly active as growth retardants. Of the active compds., 58 (11%) were also active in the pea bioassay. Only 5 of the tested compds. were shown to be antagonists of gibberellin formation in Fusarium moniliforme. Twelve of the 28 naturally occurring lactones (mostly sesquiterpenoid .gamma.-lactones), 21 of 32 lichen constituents, and a relatively large no. of the steroids tested (28 of 90) were active.

L189 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1971:142092 CAPLUS
DOCUMENT NUMBER: 74:142092
TITLE: Correlation of structure and fragmentation modes of costunolide and its derivatives
AUTHOR(S): Sathe, R. N.; Deshpande, Mrs. N. R.; Kulkarni, G. H.; Kelkar, Govind R.; Das, K. Ganesh
CORPORATE SOURCE: Natl. Chem. Lab., Poona, India
SOURCE: Organic Mass Spectrometry (1971), 5(2), 197-202
CODEN: ORMSBG; ISSN 0030-493X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mass spectral studies of costunolide and its lactone derivs., revealed general fragmentation modes involving the losses of 44, 55, 57, 59, 71, 73, and 83 mass units from the mol. ion. The genesis of these ions was established by high resolution, metastable transitions, and D labeling studies. Comparisons were made with the mass spectra of the C6-desoxy esters.

L189 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1963:482375 CAPLUS

DOCUMENT NUMBER: 59:82375
ORIGINAL REFERENCE NO. 59 15314h,15315a-h
TITLE Mexicanin. I A new sesquiterpene lactone related to tenulin
AUTHOR(S): Dominguez, E.; Romo, J.
CORPORATE SOURCE: Univ. Nacl. Autonoma Mexico, Mexico City
SOURCE: Tetrahedron (1963), 19(9), 1415-21
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB cf. CA 55, 22365f. The mother liquors from isolation of helenalin from Helenium mexicanum evapd. and the residue crystd. from C6H6 gave 430 mg. product, m. 246-53.dblvert., recrystd. from CHCl2-MeOH to yield mexicanin I (I, R = H) (II), m. 257-60.degree., [.alpha.]20D 42.5.degree. (CHCl3). (All [.alpha.]D were detd. at 20.degree. in CHCl3.) II (150 mg.) in 4 ml. 1:1 Ac2O-C5H5N heated 1 hr. on a steam bath and dild. with H2O, filtered, and the ppt. crystd. from Me2CO.Et2O gave 130 mg. I (R = Ac) (III), m. 200-3.degree., [.alpha.]D 26.5.degree.. II (150 mg.) in 20 ml. MeOH treated with CH2N2 (from 2 g. MeNHCONHNO) in Et2O 30 min. at 20 degree. and the excess CH2N2 destroyed with a few drops of AcOH, the mixt. filtered off, and the residue washed with Et2O gave 90 mg. II dipyrazoline, m. 185.degree. (decompn.). The nuclear magnetic resonance (n.m r.) spectrum of III supported the assigned structure. II (200 mg.) in 8 ml. AcOH kept 1 hr. at 20.degree. with 150 mg. CrO3 in 5 ml. 1:4 H2O-AcOH, the H2O-dild. soln. extd. with CHCl3, the ext. washed with H2O, 5% Na2CO3, and H2O, evapd., and the residue recrystd. repeatedly from Me2CO-Et2O gave dehydroisomexicanin I (IV), m. 232-5.degree., [.alpha.]D 129.degree.. II (300 mg.) in 150 ml. EtOAc hydrogenated over 80 mg. 10% Pd-C, the filtered soln. evapd , the oily residue crystd. from Et2O, and the product crystd. from Me2CO-C6H14 yielded di-hydroisomexicanin I (V), m. 144-6.degree., [.alpha.]D 150-4.degree.. The cyclo-pentanone bond was reduced but the remaining bond at C-7-C-11 resisted hydrogenation. The salient features of the spectra of II, III, IV, and V, particularly the sharp signal due to a tertiary Me group, strikingly resemble those of parthenin, tenulin, and helenalin, which possess an abnormal guaianolide nucleus. V (170 mg.) in 6 ml. AcOH treated with 150 mg. CrO3 in 5 ml. 1:4 H2O-AcOH, the mixt. kept 80 min. at 20.degree., dild. with H2O and extd. with CHCl3, the ext. washed with H2O, dried (Na2SO4), and evapd., the residue crystd. from Me2CO-C6H14, and recrystd. from Me2CO-Et2O gave dehydrodihydroisomexicanin I (VI), m. 173-5.degree., [.alpha]D 184.degree.. VI (100 mg.) in 10 ml. AcOH refluxed 3 hrs. with 800 mg. powd. Zn, the filtered soln. dild. with H2O and extd. with CHCl3, the ext. washed with H2O, 5% aq NaOH, and H2O, the dried ext. evapd., and the oily residue triturated with Et2O gave 60 mg. needles recrystd. from Me2CO-Et2O to give dehydro-deacetyldihydroisotenulin (VII), m. 168-71.degree., [.alpha.]D 20.degree.. IV (100 mg.) similarly reduced

gave 45 mg. VII, m 147-9.degree., .alpha.|D 22..degree. Differences in m.p. were apparently due to solvation. II (500 mg.) in 80 ml. C6H6 refluxed 6 hrs. with 2 ml. C5H11N and 2 ml. PhCH2SH, the cooled mixt. washed with dil. HCl and H2O, the dried soln evapd., the residual oil (760 mg.) taken up in 70 ml. alc., the soln. refluxed 8 hrs. with 7 g. freshly prepd. Raney Ni with stirring, filtered, evapd., and the oily residue crystd. from Et2O-C6H14 and recrystd. from Me2CO-Et2O gave deacetyldihydroisotenulin (VIII, R = H) (IX), m. 194-6.degree., [.alpha.]D 139.degree.. IX (60 mg.) in 2 ml. 1:1 Ac2O-C5H5N heated 1 hr. on a steam bath, the soln. poured into H2O, extd. with CHCl3, the ext. washed with dil. HCl, H2O, dil. aq. NaOH, and H2O, dried, evapd., and the oily residue crystd. from Et2O and recrystd. from Et2O-C6H14 gave dihydroisotenulin VIII (R = Ac), m. 149-50.degree., [.alpha.]D 101.degree., 1770 cm.-1 IX (40 mg.) in AcOH oxidized with CrO3 and the isolated product crystd. from Me2CO-C6H14 gave VII, m. 145-7.degree.. Accordingly, II is an "abnormal" guaianolide with asym. centers at C-1, C-5, C-8, and C-10 and lactone closure at C-8. The centers at C-6 and C-7 have the same configuration as in tetulin, but II differs from helenalin at C-6 and C-8 also, though both lactones have the same structural formula. II underwent a rearrangement in alk. medium to yield products of the "neo" type. II (140 mg.) in 20 ml. MeOH refluxed 3 min. with 140 mg. KOH in 2 ml. H2O, the mixt. kept 30 min. at 20.degree., acidified with AcOH, concd., dild. with H2O, extd. with CHCl3, and the H2O-washed ext. concd., treated with Et2O, and filtered off gave 70 mg. platelets, recrystd. from CHCl3-MeOH to give neomexicanin I (X, R = H) (XI) m 259-63 degree., [.alpha.]D 10.degree.. The mother liquor from the 1st crystn. evapd., the oily residue crystd. from Me2CO-C6H14, and the product recrystd. gave methoxydihydroneomexicanin I (XII), m. 168 70.degree., [.alpha.]D -27.degree.. Alk. treatment of II with KOH in tert-BuOH gave only XI. Acetylation of XI gave X (R = Ac), m. 170-2.degree. (Me2CO-Et2O), [.alpha]D 3.degree.; n.m.r. spectrum showed similar signals to those reported for neohelenalin and neotenulin. III (500 mg) in 60 ml. EtOAc hydrogenated over 60 mg. prereduced PtO2 4 hrs., the filtered soln. evapd., and the oily residue crystd. from Et2O and recrystd. from Et2O-C6H14 yielded 11-epidihydro-isotenulin, m. 109.degree., [.alpha.]D 48.degree.. Infrared, ultraviolet, and n.m.r. spectral data for most of the compds. were given.

L189 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1962:483404 CAPLUS
DOCUMENT NUMBER: 57:83404
ORIGINAL REFERENCE NO.: 57:16665d-i,16666a-h
TITLE: Terpenoids. XXXII. Absolute configuration of junenol and levojunenol and synthesis of junenol from costunolide
AUTHOR(S): Shaligram, A. M ; Rao, A S.; Bhattacharyya, S. C.

CORPORATE SOURCE: Nat. Chem. Lab., Poona, India
SOURCE: Tetrahedron (1962), 18, 969-77
DOCUMENT TYPE: Journal
LANGUAGE Unavailable
AB cf. CA 54, 22709d; 57, 13808e. The hydrocarbon-rich fraction (b0 5 90-102.degree.) of distd. vetiver oil chromatographed on acid-washed Al2O3 (grades III and II) and the tail portion crystd. from pert. ether and sublimed gave levojunenol (I), m. 65.degree., [.alpha.]D -57.degree. (I 1.18, all rotations in 95% alc.). I (298 mg.) heated (N atm) 16 hrs. at 290.degree. with 446 mg. Se and the product taken up in petr. ether-C6H6, the concd. filtrate filtered through 30 g. Al2O3 (grade I) and eluted with petr. ether gave 228 mg. endalene, characterized as picrate, m. 95-6.degree., and s-trinitrobenzene deriv., m. 112.5-13.0.degree. I (1 024 g.) in 25 ml AcOH hydrogenated 4 hrs. with 40 mg. prereduced PtO2 and the product (970 mg.) sublimed gave dihydrolevojunenol (II), m. 115.degree.. [.alpha.]D .+-.0 degree. (C 2.6). I (970 mg.) in 60 ml. dry EtOAc at -5.degree. ozonized 5 hrs. with evolution of HCHO and the mixt. evapd. at 40.degree. in vacuo, the ozonide decompd. by heating in 30 ml. H2O on a steam bath 4 hrs. and the aq. layer extd. with Et2O, washed with aq. NaHCO3 and the neutral product isolated, the liquid residue (820 mg.) distd. at 135.degree. 0.1 mm and the solid product sublimed gave 740 mg. oxo alc. (III), C14H22O2, m 43.degree., [.alpha.]D -11.5.degree. (c 2.00). The properties of I and its derivs. agree with those of an optical antipode of the dextrorotatory alc., junenol. III (420 mg.) in 4 ml. (HOCH2CH2)2O heated (N atm.) 2 hrs. with 400 mg. KOH and 0.7 ml. 85% N2H4.H2O at 110-15.degree. with occasional shaking and the H2O evapd. at 195.degree., the mixt. refluxed 4 hrs. at 190.degree. and the cooled product dild. with 30 ml. H2O, neutralized at 0.degree. with dil. HCl and extd. with Et2O, the ext. neutralized and the dried soln. evapd., the product (383 mg.) dehydrogenated with 530 mg. Se at 280.degree. and the product chromatographed over 30 mg. Al2O3 (grade I) gave 2-Me2CHC10H7, characterized as s-trinitrobenzene deriv., m. 107 degree.. Santanolide a (11.3 g., prepd. according to Kovacs, et al., CA 50, 11285f, from L-santonin) in 100 ml. Et2O stirred at -10.degree. 1 hr. with addn. of 435 mg. LiAlH4 in 100 ml. dry Et2O and the mixt. stirred 2 hrs. before warming to 20.degree., the mixt. decompd. with H2O and extd. with Et2O gave 10.2 g. amorphous material showing a pos. Fehling test. The reduced product (3.17 g.) taken up in 14 ml. distd. (HOCH2CH2)2O and shaken 30 min. at 20.degree. with 6 ml. 85% N2H4.H2O, the soln. refluxed 2 hrs. (N atm.) with 3 g. KOH at 110-15.degree. and the H2O evapd. at 195.degree., the soln. refluxed 3 hrs. at 190.degree. and the cooled product dild. with 50 ml. H2O, repeatedly extd. with Et2O and the residue on evapn. (700 mg.) chromatographed over 30 g. Al2O3 (grade III), eluted with 200 ml 9:1 petr. ether-C6H6 and the fraction sublimed gave 388 mg. alc., C15H28O (IV), m. 53-4.degree.. As expected, the infrared spectrum of IV differed from that of II, and the same series of reactions was applied to

santanolide c (V). Costunolide (21.4 g., m. 106.degree.), [.alpha.]D 128 degree. in 200 ml. AcOH contg. 10 ml. 65% HClO4 hydrogenated with prereduced PtO2 and the filtered soln. concd. to 70 ml., neutralized with Na2CO3 and extd. with Et2O gave 6.3 g. V, m. 153-4.degree. (alc.), [.alpha.]D 54.9 degree , also prepd. by hydrogenating a mixt. of costunolide and dehydrocostus lactone. V (9.9 g.) in 100 ml. Et2O partially reduced with 500 mg. LiAlH4 in 100 ml. Et2O and totally reduced by Huang Minlon reduction gave material, purified by chromatography and sublimation to yield 379 mg. alc. (VI), m. 115.degree., [.alpha.]D +-. 0.degree. (c 1.52), giving an infrared spectrum completely superimposable on that of II, and an identical n.m.r. spectrum, showing that VI and II are either identical or enantiomorphic. Mixed m.p. of VI and II gave a 20.degree. depression and the lack of identity was confirmed by measurement or rotatory dispersion curves. The mol. rotation difference (.DELTA.M = -129.degree.) between I and II is neg. but of the same magnitude as that between junenol (VII) and VI, which is of the same sign as that between eudesmol and dihydroeudesmol. Accordingly the abs. configuration of VII, I, and II can be depicted. I is the 1st naturally occurring eudesmanic compd. contg. both .alpha.-oriented C-10 Me and C-7 Me2CH groups. The acid cyclization of dihydrocostunolide (VIII) gave a mixt. of 2 closely related lactones, the endocyclic unsatd. lactone (IX) and the exocyclic unsatd. isomeride (X), sepd. by column chromatography. VIII (m. 77.degree , [.alpha.]D 113.degree.) cyclized in AcOH and Ac2O and the mixt. (62 g.) chromatographed on 2.4 kg. Al2O3 (grade III) and eluted successively with 10 l. petr. ether, 6 l. 1:1 petr. ether-C6H6, 6 l. C6H6, 6 l. alc., and 6 l. AcOH gave 27 g. fraction, m. 128.degree.; 0.8, 0.5, and 0.5 g. fraction, m. 60 degree.; and 24.5 g. fraction, m. 132.degree.. The 1st fraction repeatedly recrystd. from alc. and C6H14 and sublimed gave IX, m. 140.degree., [.alpha.]D 85 degree. (c 1.402, CHCl3), hydrogenated in AcOH with prereduced PtO2 to give V. The last fraction recrystd from C5H12 and sublimed gave the lactone X, m. 140.degree. [.alpha.]D 140.degree. (c 3 5, CHCl3), hydrogenated in AcOH with prereduced PtO2 to give santanolidea. X (1.1 g.) in 30 ml dry EtOAc ozonized 5 hrs. at -5.degree. with evolution of HCHO, the product crystd. from alc. and sublimed at 150.degree /0.05 mm. gave 800 mg. oxo lactone (XI), m. 220.degree [.alpha.]D 71.48.degree. (c 1.525, CHCl3). X (7.15 g.) in 150 ml. anhyd. Et2O at -10.degree. stirred 1 hr. with addn. of 420 mg. LiAlH4 in 100 ml. Et2O and the mixt. stirred 2 hrs. at -10.degree. and 1 hr. at 20.degree., the washed and dried Et2O layer evapd. in vacuo and the partially reduced lactone (6.8 g.) heated 5 min. on a steam bath in 40 ml (HOCH2CH2)2O and 11 ml. 85% N2H4.H2O, the clear soln. kept 30 min. at 20 degree. and refluxed 2 hrs. at 110-15.degree. with 6 g. KOH, treated at 60.degree. with 20 ml. dry C6H6 and the C6H6 carefully evapd. at 130.degree. the procedure repeated 3 times and the H2O-free soln. refluxed 2 hrs. at 150.degree., the cooled mass dild. with 50 ml. H2O and extd.

with Et2O, the product (800 mg.) chromatographer on 30 g. Al2O3 (grade III) and the column eluted with 200 ml. 9:1 petr. ether-C6H6, the fraction crystd. from petr. ether and sublimed gave VII, m. 61-2.degree., [.alpha.]D 51.degree. (C 2.45). Ultraviolet, infrared, and nuclear magnetic resonance spectra were given.

L189 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1961:137670 CAPLUS
DOCUMENT NUMBER: 55:137670
ORIGINAL REFERENCE NO.: 55:26013g-i,26014a-i,26015a-i,26016a-d
TITLE: Cedrol stereochemistry and total synthesis
AUTHOR(S): Stork, Gilbert; Clarke, Frank H., Jr.
CORPORATE SOURCE: Columbia Univ.
SOURCE: J. Am. Chem. Soc. (1961), 83, 3114-25
CODEN: JACSAT; ISSN 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue
AB The total stereospecific synthesis of natural cedrol (I) was described. Me2C(CN)CH(CN)CO2Et (II), b0.01 about 99-114.degree., b4 120-7.degree. (with decompn.), (250 g.) in 232 g. Me3COH treated with 87 g. CH2:CHCN and 5.0 cc. 40% choline in MeOH, the mixt. kept 6 hrs. at 0.degree., 18 hrs. at room temp., and 40 hrs. at 50.degree., cooled until crystals of Me3COH appeared, the top layer evapd on the steam bath in vacuo, the combined residue and bottom layer dild. with Et2O, washed, evapd., the combined residues (638 g.) from 2 runs dissolved in 1300 cc. concd. HCl and 1300 cc. H2O, the soln. refluxed 48 hrs., evapd. on the steam bath, cooled, filtered, evapd. to dryness, the residue treated with abs. EtOH, filtered, the filtrate (3500 cc.) refluxed 4.5 days with stirring with 700 cc. concd. H2SO4, 1 l. of EtOH distd., the residual soln. cooled, poured into satd. aq. NaCl, the oily layer worked up with Et2O, and distd. gave 480 g. Me2C(CO2Et)CH(CO2Et)(CH2)2CO2Et (III), b0.01 about 154-6.degree., and 158 g. residue, which hydrolyzed and reesterified gave more III. III refluxed 3 hrs. in C6H6 with powd. Na yielded 64% di-Et 3,3-dimethylcyclopentan-2-one-1,4-dicarboxylate (IV), b. 132-3.degree (in vacuo). PhCH2OH (34.0 g.), 48 g. MeCHBrCO2H, and about 0 5 g. p-MeC6H4SO3H in 150 cc. C6H6 refluxed 18 hrs. with azeotropic removal of H2O gave 55.5 g. MeCHBrCO2CH2Ph (V), b7 139-41.degree.. IV (50.0 g.) in 80 cc. dry C6H6 and 6.0 g. NaH in 100 cc. dry C6H6 refluxed until the H evolution ceased, decanted, the soln. distd. to remove 155 cc C6H6, treated with the Na salt of 47.5 g. V in 100 cc. dry HCONMe2, the mixt. heated at 50 degree. under N, kept 1 week, combined with the soln. of a 2nd run from 71 .1 g. IV, and worked up yielded 179 g. 1-PhCH2 ester (VI) of the HO2CCHMe deriv. (VII) of IV, b. 175-92.degree. (in vacuo). VI (77.0 g.) in 150 cc. EtOAc hydrogenolyzed during 35 min. over 8.0 g. 10% Pd-C at an initial pressure of 50.0 lb. yielded 47.0 g. VII, prisms, m. 113-15.degree.

(cyclohexane). Na salt (11.6 g.) of VII in 100 cc. dry C6H6 contg 1.0 cc. C5H5N with 15 cc. (COCl)2 added slowly to excess CH2N2 in Et2O from 45 g. H2NCON(NO)Me, the mixt. kept 1 hr. at 0.degree., evapd. on the steam bath, and the residual crude diazoketone treated in 150 cc. dry Et2O with cooling with dry HCl gave 10.7 g. 1-ClCH2COCHMe deriv (VIII) of V, m. 72-3.degree. (cyclohexane). VIII (19.2 g.) and 20 g. powd. KI in 250 cc. AcOH treated slowly with stirring at 25.degree. with 100 g. Zn dust, stirred 6 hrs., dild. with 50 cc. H2O, stirred overnight, filtered, the filtrate evapd., the residue partitioned between H2O and Et2O, and the Et2O soln. worked up gave 17.1 g. 1-AcMeCH deriv. (IX) of V, m. 55-60.degree. (petr. ether), semicarbazone m. 191-3.degree. (aq. EtOH). Crude IX (4.3 g.) in 30 cc. dry Me3COH and 0.7 g. K in 70 cc. dry Me3COH refluxed 3 hrs. under N, dild. with H2O, and extd. with Et2O gave 1.47 g. mobile oil; a 0.4-g. portion, 0.45 g. semicarbazide, 1.65 cc. C5H5N, and 8 cc. EtOH refluxed 1.5 hrs. and kept overnight yielded the semicarbazone of X, m. 174-6.degree. (EtOAc-cyclohexane). IX (20.1 g.) and 3.0 g. K in 300 cc. dry Me3COH kept 10 min. at room temp. gave 18.6 g. crude aldol, which, refluxed 1 hr. with 2.0 g. p-MeC6H4SO3H.H2O in 400 cc. C6H6, yielded 15.2 g. XI, m. 46-56.degree. (petr. ether), 23.6 g. crude XI recrystd. twice from petr. ether gave 10.8 g. of 1 isomer, m. 65-7.degree., of XI. XI (504 mg.), m. 65-7.degree., in 16 cc. abs. EtOH hydrogenated 20 min. at 25.4.degree. over 136 mg. 10% Pd-C yielded 325 mg. XII, m. 33.5-35.0.degree. (petr. ether); 2,4-dinitrophenylhydrazone (XIII) m. 160-1.degree.; recrystd. from EtOAc-EtOH, it gave needles, which slowly changed to prisms on standing in the soln. XI (307 mg.) in 2 cc. dry tetrahydrofuran and 15 cc. dry liquid NH3 treated with stirring with 15-20 mg. Li and then with 0.6 g. NH4Cl, the NH3 evapd., and the residual yellowish oily XII (271 mg.) chromatographed from petr. ether on Al2O3 yielded oily colorless XII; XIII m. 152-4.degree. (EtOAc-EtOH). XII (655 mg.) in 10 cc. 80% EtOH refluxed 36 hrs. under N with 2.0 g. KOH, poured into H2O, washed with Et2O, acidified with concd. HCl, extd. with Et2O, the gummy residue (528 mg.) from the ext. refluxed 3 hrs. with 6 cc. Ac2O, evapd. under a stream of N, and the dark residue sublimed in vacuo at 160-70.degree. gave 174 mg. anhydride (XIV), prisms, m. 171-3.degree. (Et2O). The XIV refluxed 20 hrs. with 6 cc. 50% aq. dioxane and the oily product treated with MeCHN2 from 5 cc. EtO2CN(NO)Et yielded 102 mg. XII; XIII m. 159-61.degree.. XII (1.03 g.) in 10 cc. CHCl3 and 1.0 cc. (CH2SH)2 satd. with dry HCl and kept at 0.degree. overnight yielded 0.86 g. XV, m. 75-6.degree. (pentane). XV (1.32 g.) in 125 cc. abs. EtOH stirred 15 hrs. at reflux with 50 g. Raney Ni alloy gave 0.86 g. di-Et ester (XVI) of dl-norcedrenedicarboxylic acid (XVII), mobile oil. XVII (0.82 g.) and 2.0 g. KOH in 10 cc. 95% EtOH refluxed 24 hrs., poured into H2O, and acidified with 10 cc. concd. HCl gave 0.62 g. XVII, m. 221-3.degree. (Et2O-pentane). XVII (300 mg.) in Me2CO with 410 mg. quinine in acetone yielded 252 mg. quinine salt (XVIII) of (-)-XVII, m. 209-10.degree. (CHCl3Me2CO), [.alpha.]27D -122.degree. (c 1.00, CHCl3).

XVII (121 mg.) shaken 15 min. with 5 cc. 6N HCl gave 46 mg (-)-XVII, m. 212-13.degree., [.alpha.]27D -38.9 .+-. 1.5.degree. (c 1.08, Me2CO); natural (-)-XVII m. 213-14.degree., [.alpha]27D -38.3 .+-. 1.0 degree. (c 1.09, Me2CO). (-)-XVII (10.00 g.) with excess CH2N2 in Et2O yielded 10.59 g. XIX (R = CO2H) (XX), b1 95-132 degree . XX (10.5 g.) and 2.4 g. KOH in 35 cc. abs EtOH refluxed 2 hrs. gave about 2 g. unchanged XX and 6.20 g. XIX (R = CO2Me) (XXI), m. 129-32 degree . XXI (8.05 g.) and 20 cc. (COCl)2 kept 1.5 hrs. at room temp , dild., evapd. with C6H6, the residual XIX (R = COCl) treated 1 hr with CH2N2 from 45 g. H2NCON(NO)Me in Et2O, the resulting crude XIX (R = CON2) in 50 cc. dry Et2O satd with dry HCl, evapd. in vacuo on the steam bath, the XIX (R = COCH2Cl) treated with cooling and stirring with 9 g. KI in 100 cc. 80% AcOH and 45 g. powd. Zn, and the mixt. stirred at room temp. overnight yielded 7.73 g. crude XIX (R = Ac) (XXII); 2,4-dinitrophenylhydrazone m. 140-2.degree. (cyclohexane). XXII (7.73 g.) and 3.0 g. KOH in 120 cc. dry Me3COH refluxed 3 hrs. yielded 4.90 g. XXIII, m. 202-4.degree (dioxane) XXIII (2.00 g.) refluxed 17 hrs. with stirring with 2.00 g LiAlH4 in 50 cc. dry Et2O gave 1.91 g. (crude) XXIV, m. 120-1.degree (cyclohexane). Crude XXIV oxidized with CrO3-C5H5N and the crude product chromatographed on Al2O3 yielded XXV; 2,4-dinitrophenylhydrazone m. 146-7.degree.. XXIII (2.84 g.) in 50 cc. abs. EtOH contg. 0.10 g. p-MeC6H4SO3H H2O distd. during 4 hrs to remove 53 cc. distillate gave 2.82 g. oily mixt. of the enol ethers, the crude mixt. in 25 cc. dry Et2O reduced with 1.0 g LiAlH4 in 150 cc. Et2O and the crude product (2.45 g.) refluxed 1.5 hrs. with 0.20 g. p-MeC6H4SO3H H2O in 50 cc. C6H6 yielded 508 mg. XXIV. XXIII (5.21 g.) in dry Et2O reduced with 7.77 g. LiAlH4 in 250 cc. dry Et2O, the crude foamy product (4.11 g.) treated 17 hrs. at room temp. with 8.43 g. CrO3 in 84 cc. C5H5N, the mixt. poured into 750 cc. Et2O, filtered, and the filtrate worked up gave 2.81 g. pale yellow oily aldehyde-ketone; a 2.50-g. portion refluxed 1.45 hrs. with 12.5 g. KOH in 500 cc. H2O at about 50.degree. and 90 mm., extd. with Et2O, and the crude oily product (2.02 g.) chromatographed on Al2O3 yielded 1.47 g. XXVI; 2,4-dinitrophenylhydrazone, brilliant red prisms, m. 164-7.degree. (MeOH) XXVI (527 mg.) in 10 cc. abs. EtOH hydrogenated 1 hr. at 23.degree. gave 524 mg. oily XXV; 2,4-dinitrophenylhydrazone, yellow needles changing to prisms on standing in soln., m. 146-7 degree. (MeOH). XXIV (219 mg.) in 2.2 cc. C5H5N treated 23 hrs. at room temp. with 224 mg CrO3 in 2.2 cc. C5H5N yielded 190 mg. XXV. XXV (164 mg) reduced during 17 hrs. with 0.40 g. LiAlH4 in 30 cc. Et2O gave 140 mg XXIV. XXV (446 mg) in dry Et2O added slowly to MeLi from 1.8 g. Li and 6 cc. MeI in 40 cc dry Et2O and the mixt. refluxed 18.5 hrs with stirring gave I, collected in 4 fractions: 380 mg , m. 80-1.degree.; 340 mg., m. 83-7 degree.; 284 mg., m. 85-7.degree.; 215 mg., m. 86-7.degree., needles, [alpha.]28D 10.5 +-. 0.8 degree. (c 5.00); natural I m. 86-7.degree , [alpha.]28D 9.9 .+-. 0.4.degree. (c 5.00, CHCl3).

L189 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER 1962:38646 CAPLUS
DOCUMENT NUMBER: 56:38646
ORIGINAL REFERENCE NO.: 56:7368c-i
TITLE: CXXXI. Isolation and structure of costunolide , balchanolide, isobalchanolide, and hydroxybalchanolide, sesquiterpenic lactones of germacrane type from Artemisia balchanorum
AUTHOR(S): Krasch, H.; Herout, V.; Suchy, M.; Sorm, F.
CORPORATE SOURCE: Ceskoslov. Akad. Ved., Prague
SOURCE: Collection Czechoslov. Chem. Communs. (1961), 26, 2612-23
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB Costunolide (I), m. 106.degree. (MeOH), [.alpha]20D 128.degree. (c 10.5. CHCl3), isobalchanolide (II), m. 133.degree. (iso-Pr2O-Me2CO), [.alpha.]20D 122.degree. (c 2.08, CHCl3), balchanolide (III), m. 154.degree. (iso-Pr2O-Me2CO), [.alpha.]20D 183.degree. (c 1.84, CHCl3), and hydroxybalchanolide (IV), m. 163.degree. [.alpha.]20D 105.degree (c 2.71, EtoH). Hydrogenation of I in MeOH over 5% Pd on C gave dihydrocostulolide (V), m. 79-80.degree. (MeOH). Hydrogenation of I in AcOH over PtO2 gave oily hexahydrocostunolide. If 2 drops of 70% HClO4 were added to the mixt., the H uptake amounted to 2.0 double bonds and santanolide C (VI) was the chief product, m. 155.degree. (EtOH), [.alpha.]20D 50.1.degree. (c 4.0, CHCl3), along with 2 compds., m. 114.degree. (MeOH) and m. 79 degree., isolated by chromatography. Refluxing V with AcOH and Ac2O, evapg. the mixt., and crystg. from MeOH gave a compd., m. 122.degree., whose recrystn. from 1 5 C6H6-petr ether gave 3-santenolide (VII), m. 135.5.degree.. Hydrogenation of VII in AcOH over PtO2 (H uptake amounted to 1.05 double bonds) followed by crystn. and chromatography gave VI along with santanolide A, m. 153.degree. (80% aq. EtOH). The location of the double bonds in I (CA 54, 3489b) was verified by ozonization of V in AcOH and decompn. of the ozonides in boiling HNO3: the chief product, a lactonedicarboxylic acid, Rf 0.38 (BuOAc-2% HCO2H), was identical with that prepd. earlier from artabsin. Acetylisobalchanolide, m. 139-40.degree., [.alpha.]20D 18.5.degree. (c 1.8, CHCl3), was hydrogenated in MeOH over PrO2 to give tetrahydroacetylisobalchanolide (VHI), m. 125.degree. (iso-Pr2O), identical with tetrahydroacetylbalchanolide, prepd. earlier. Hydrolysis of VIII with K2CO3 in MeOH followed by oxidn. of the oily product with CrO3 in AcOH gave an oxo lactone, C15H24O3, m. 136 5.degree. (iso-Pr2O), identical with that prepd. earlier from arctiopicrin and cnicin. Oxidn. of II-IV with satd. aq. KMnO4 gave a mixt. of (CH2CO2H)2 and MeCOCH2CH2CO2H, identified by paper chromatography. Oxidn. of III with CrO3 in C5H5N gave an oxo lactone, C15H20O3, m 110.degree (iso-PrO2).

Hydrogenation of IV in AcOH over PtO2 gave tetrahydrohydroxybalchanolide C15H26O4, m. 101.degree. (iso-Pr2O-Me2CO), whose oxidn. with CrO3 in AcOH gave a hydroxy oxo lactone, C15H24O4 (IX), m. 127.degree. (isoPr2O-Me2CO). Structures of II-IV and some of their derivs. were suggested. II and III differ in the location of the double bonds, or, in their steric arrangement (cis-trans-isomerism) only.

L189 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1962:423334 CAPLUS
DOCUMENT NUMBER: 57:23334
ORIGINAL REFERENCE NO. 57:4699b-g
TITLE: Conversion of costunolide to junenol
AUTHOR(S): Shaligram, A. M.; Rao, A. S.; Bhattacharyya, S. C.
CORPORATE SOURCE Natl Chem. Labs., Poona, India
SOURCE: Chem. Ind. (London) (1961) 671
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB (All [.alpha.]D in EtOH.) Previously (CA 54, 22709d) the abs. configuration was established of the enantiomeric sesquiterpene alcs. junenol (I) and levojunenol (II), on the basis of conversion of santanolide c (III) to dihydrojunenol (IV). The structure and conversion of the lactone V to dextrorotatory I was now described. Cyclization of VI gave a product (VIa), m. 117.degree., much lower than that of the lactone (VII), previously (CA 54, 3489d) obtained by cyelization of VI. Chromatography of Via gave VII, m. 140.degree., [.alpha.]D 85.degree. (c 1.402), giving III on catalytic hydrogenation, giving no CH2O on ozonolysis, this structure also being in agreement with its infrared (v 790 and 1794 cm.-1) and ultraviolet spectra (.epsilon.210 287, .epsilon.2151435, .epsilon.220 385), and an isomer (V), m. 140.degree., [.alpha.]D 140.degree. (c 3.55), this structure being assigned on the basis of infrared (v 885, 1633, and 1764 cm.-1) and ultraviolet spectra (.epsilon.210 377, .epsilon.215 120, .epsilon.220 75), giving santanolide a on catalytic hydrogenation, giving on ozonolysis CH2O (dimedon deriv. m. 189.degree.) and the oxo lactone (VIII), m. 210.degree., [.alpha.]D 71.degree. (c 1.525). V was converted to d-I as described previously for the conversion of III to IV. d-I m. 61-2.degree., [.alpha.]D 51.degree. (c 2.45), its infrared spectrum being identical with that of II.

L189 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1950:711 CAPLUS
DOCUMENT NUMBER: 44:711
ORIGINAL REFERENCE NO.: 44:138f-i,139a-b
TITLE: Helenalin. I. Isolation and properties
AUTHOR(S) Adams, Roger; Herz, Werner

SOURCE: J. Am. Chem. Soc. (1949), 71, 2546-51
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE Journal
LANGUAGE: Unavailable
AB cf. Clark, C.A. 30, 8236.2. Helenalin (I), C15H18O4, was isolated from Helenium microcephalum by the method of C. in av. yields of 0.38% and, crystd 3 times from abs. EtOH, m 176-8.degree.; the residue, crystd. 3 times from abs. EtOH, m 165.5-6.degree , [.alpha.]D25 -102.8 degree. (0.0728 g. in 2 ml. 95% EtOH), the infrared spectrum is identical with that of C.'s prepn. The Ac deriv. (II), m. 179.5-80.5.degree , absorption max. at 221 and 316 m.mu. (.epsilon. 12, 600 and 61). o-Bromobenzoyl deriv. of I, m. 162-3.degree.; p-nitro-benzoyl deriv. of I, with 0.5 mol. C6H6, m. 111.degree.; 3,5-dinitrobenzoyl deriv., with 0.5 mol. C6H6, m. 213.degree.. Tetra-hydrohelenalin (III), m. 175-6.degree., infrared spectrum given; Ac deriv. (IV), m. 145.degree. (prepd. by acetylation of III or by reduction of II in AcOEt over Pt oxide); the spectra of III and IV are similar [absorption max. at 287 m.mu. (.epsilon. 36)]. IV (115 mg.) and 64 mg. piperonal in 2 ml. abs. EtOH, treated with 5 ml. satd. EtOH-HCl and kept 18 hrs., give the piperonylidene deriv. of II, C25H25O7Cl, pale yellow, m. 214.degree.. I (50 mg.) in 1 ml. AcOH, treated with 1.03 g. Br in 15 ml. AcOH at room temp., gives 71 mg dibromohelenalin (V), decomp. 130.degree.; recrystn. of V from 50% EtOH or 50% AcOH gives bromohelenalin, m. 164.5.degree., absorption max. at 248 and 314 m.mu. (.epsilon. 6300 and 97); reduction over Pt oxide gives III. II and Br in Ac-OH, irradiated with an elec. light, give a di-Br deriv., decomp. 153-4.degree.; boiled 0.5 hr. with 50% EtOH, it gives the Br deriv., m. 153.5.degree.. I and NH2OH.HCl in abs. EtOH contg. AcONa, refluxed 16 hrs., give the compd. C15H22N2O5, amorphous, m. 200-3.degree. (decompn.). I (1 g.) and 4 g. (iso-PrO)3Al in 20 ml. iso-PrOH, refluxed 5 hrs., the solvent removed by slow distn., 20 ml. iso-PrOH added, the distn. continued until the test for Me2CO is neg., the product decompd. with 25 ml. 10% H2SO4, and extd. with ether, give 100 mg. of the compd., C15H20O4, b0.1 200-30.degree. (bath temp.); it did not yield a solid ester; in 1 expt. there resulted 29 mg. of a compd., m. 196-201.degree., which may be an intramol. oxidation-reduction product. I and O3 give 50-60% HCHO; II gives 45% HCHO. Chem. and phys. evidence establishes the presence of the grouping RCOCH:CR2, possibly a part of a 5-membered ring, and makes likely the presence of a lactone ring. These functional groups account satisfactorily for all 4 O atoms and for 1 of the double bonds. The other double bond is unconjugated and part of a terminal CH2 group.

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
ACCESSION NUMBER: 2002:107101 CAPLUS
DOCUMENT NUMBER: 136:161354
TITLE: Terpene compound compositions exhibiting synergistic inhibition of the expression and/or activity of cyclooxygenase-2, and use as antiinflammatory agents
INVENTOR(S): Babish, John G.; Howell, Terrence M.; Pacioretty, Linda M.
PATENT ASSIGNEE(S): Ashni Naturaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009698	A1	20020207	WO 2001-US24053	20010801

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002077359	A1	20020620	US 2001-919510	20010731

PRIORITY APPLN. INFO.: US 2000-222190P P 20000801
US 2001-919510 A 20010731

AB A formulation is provided that serves to inhibit the inflammatory response in animals. The formulation comprises, as a first component, a **diterpene triepoxide lactone** species or a **sesquiterpene lactone** species and, as a second component, at least one member selected from the group consisting of a **diterpene triepoxide lactone** species, a **sesquiterpene lactone** species, a diterpene **lactone** species, and a triterpene species or derivs. thereof, with the proviso that the same first component cannot also serve as the second component, and provides synergistic antiinflammatory effects in response to phys. or chem. injury or abnormal immune stimulation due to a biol. agent or unknown etiol.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
ACCESSION NUMBER: 2002:466702 CAPLUS
DOCUMENT NUMBER: 137:41737
TITLE: Combinations of **sesquiterpene lactones** and **diterpene triepoxide lactones** for synergistic inhibition of cyclooxygenase-2
INVENTOR(S): Babish, John G.; Howell, Terrence; Pacioretty, Linda
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 18 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002077299	A1	20020620	US 2001-919349	20010731
US 2002076452	A1	20020620	US 2001-919506	20010731

PRIORITY APPLN. INFO.: US 2000-222167P P 20000801

AB A novel formulation is provided that serves to inhibit the inflammatory response in animals. The formulation comprises, as a first component an effective amt. of **diterpene triepoxide lactone** species and an effective amt. of a second component of **sesquiterpene lactone** species or derivs. thereof, and provides synergistic anti-inflammatory effects in response to phys. or chem. injury or abnormal immune stimulation due to a biol. agent or unknown etiol. For example, a lotion designed to contain 0.1 % triptolide and 0.1% parthenolide was applied to affected areas of patients with acne rosacea and results showed improvement as compared with the placebo control.

L6 ANSWER 3 OF 3 IFIPAT COPYRIGHT 2003 IFI DUPLICATE 3

AN 10133723 IFIPAT;IFIUDB;IFICDB

TITLE: COMPOSITIONS EXHIBITING SYNERGISTIC INHIBITION OF THE EXPRESSION AND/OR ACTIVITY OF CLYCLOOXYGENASE-2; FOR THERAPY OF INFLAMMATION

INVENTOR(S.): Babish; John G., Brooktondale, NY, US
Howell; Terrence, Dryden, NY, US
Pacioretty; Linda, Brooktondale, NY, US

PATENT ASSIGNEE(S.): Ashmi Naturaceuticals, Inc.

AGENT: THORPE NORTH WESTERN, 8180 SOUTH 700 EAST, SUITE 200, P.O. BOX 1219, SANDY, UT, 84070, US

	NUMBER	PK	DATE
PATENT INFORMATION:	US 2002077350	A1	20020620
APPLICATION INFORMATION:	US 2001-919510		20010731

	NUMBER	DATE
PRIORITY APPLN. INFO.:	US 2000-222190P	20000801 (Provisional)
FAMILY INFORMATION:	US 2002077350	20020620

DOCUMENT TYPE: Utility
Patent Application - First Publication

FILE SEGMENT: CHEMICAL
APPLICATION

NUMBER OF CLAIMS: 38 6 Figure(s).

DESCRIPTION OF FIGURES:

FIG. 1 illustrates the general chemical structure of (A1) the diterpene tripoxide **lactone** genus and (A2) triptolide as a species within that genus.

FIG. 2, (A1) and (A2) respectively, illustrate the general chemical structures of the **sesquiterpene lactone** genus and parthenolide as a species within that genus.

FIG. 3 (B1) and (B2) respectively illustrate the general chemical structures of the diterpene **lactone** genus and andrographolide as a species within that genus.

FIG. 4 (C1), (C2) and (C3) respectively, illustrate the general chemical structures of the triterpene genus and ursolic acid and oleanolic acid as species within that genus.

FIG. 5 provides a schematic for the experimental design of EXAMPLE 1.

FIG. 6(a)-(g) are line graphs depicting the percent inhibition of COX-2 enzyme protein expression by individual and the combinations of the tested materials, as described in EXAMPLE 17, in the absence and presence of arachidonic acid

(AA).

AB A novel formulation is provided that serves to inhibit the inflammatory response in animals. The formulation comprises, as a first component, a **diterpene triepoxide lactone** species or a **sesquiterpene lactone** species and, as a second component, at least one member selected from the group consisting of a **diterpene triepoxide lactone** species, a **sesquiterpene lactone** species, a diterpene **lactone** species, and a triterpene species or derivatives thereof with the proviso that the same first component cannot also serve as the second component., and provides synergistic anti-inflammatory effects in response to physical or chemical injury or abnormal immune stimulation due to a biological agent or unknown etiology.

CLMN 38 6 Figure(s).

FIG. 1 illustrates the general chemical structure of (A1) the diterpene tripoxide **lactone** genus and (A2) triptolide as a species within that genus.

FIG. 2, (A1) and (A2) respectively, illustrate the general chemical structures of the **sesquiterpene lactone** genus and parthenolide as a species within that genus.

FIG. 2 (B1) and (B2) respectively illustrate the general chemical structures of the diterpene **lactone** genus and andrographolide as a species within that genus.

FIG. 2 (C1), (C2) and (C3) respectively, illustrate the general chemical structures of the triterpene genus and ursolic acid and oleanolic acid as species within that genus.

FIG. 3 provides a schematic for the experimental design of EXAMPLE 1.

FIG. 4(a)-(g) are line graphs depicting the percent inhibition of COX-2 enzyme protein expression by individual and the combinations of the tested materials, as described in EXAMPLE 17, in the absence and presence of arachidonic acid (AA).